

REMARKS

1. This is in response to the Office Action mailed 10/01/02. Claims 1, 5-8, and 11-18 remain pending in this application.

2. Applicant has amended claim 1 by inserting the proper name in the first occurrence of the term (TGF), as suggested by the Examiner, in order to overcome the claim objections.

3. Applicant requests reconsideration of the rejections under 35 USC 101. Applicant has amended the claims to be process claims, incorporating a description of steps in the process.

4. Applicant requests reconsideration of the rejections under 35 USC 112, first paragraph. Applicant has enclosed a Declaration regarding the sufficiency of the disclosure and how, when combined with that known to those with skill in the art, it would allow one with such skill to carry out the invention without undue experimentation.

5. Applicant requests reconsideration of the rejections under 35 USC 102.

Referring to the document "Logan", our client has submitted the following arguments: "Logan" describes that TGF- $\beta$  is one of the positive prime regulators of the extracellular matrix production and so far leads to scar-formation after injuries (cf. Page 6, lines 16 to 23, of "Logan"). "Logan" describes that the scar blocks the reconnection of damaged neuronal pathways and to that extent prevents the stimulus transport from neuron to neuron (cf. Page 7, lines 6 to 10, of "Logan"). This effect can be blocked by an agent that inhibits the extracellular matrix producing activity of TGF- $\beta$  (cf. Page 8, lines 20 to 23, of the present application). To the contrary, according to the present invention, a compound is used for inhibiting the biological activity of TGF- $\beta$  thereby allowing the survival of neuronal cells independently whether an injury has taken place or not. In this context, it should be noted that survival means prevention of cell death, and prevention of scar formation means prevention of inappropriate matrix formation and uncontrolled cell proliferation (cf. Page 4, lines 18 to 27, of "Logan").

Furthermore, "Logan" describes the treatment of complete nerve cords damage by an injury by TGF- $\beta$  inhibitors, in contrast thereto, according to the present invention only single neurons

predamaged by a cerebral disorder are treated therapeutically by TGF- $\beta$  inhibitors.

Moreover, "Logan" describes the role of TGF- $\beta$  in CNS wounds (cf. Page 5, lines 26 to 28, of "Logan"), but the present invention describes the treatment of cerebral disorders.

In order to differentiate the present application from "Logan", claim 1 of the present application may contain the following wording "...a compound capable of substantially imparting protection and survival of predamaged neurons by inhibiting the biological activity of TGF- $\beta$ ..." (cf. Page 2, lines 20-22 of the present application). Claim 1 has been amended accordingly. Examples of categories of compounds that inhibit this activity include (1) an antibody to TGF- $\beta$ , (2) an antagonist to TGF- $\beta$ , and (3) a compound capable of altering TGF- $\beta$ . These were disclosed on page 2, lines 22-29 of the PCT application. New claim 14 has been introduced to claim these specific categories of compounds.

Referring to the document "Melton", our client has submitted the following arguments: Melton generally describes that antagonists against growth factors of the TGF- $\beta$  family induce the

differentiation of ectodermal cells to neuronal cells (instead of differentiation to mesodermal or epidermal cells). In experiments it could be shown that blocking the activin receptor (to which also other TGF- $\beta$  family members bind) leads to a neuronal differentiation of the cells. Accordingly, an activin antagonist can be efficiently used to increase differentiation and survival of neurons. "Melton" generalizes these results for the whole TGF- $\beta$  family, but is completely silent about the effect of TGF- $\beta$ 1, TGF- $\beta$ 2 and TGF- $\beta$ 3 claimed in the present application. The client proposes to argue that a method using a specific compound is novel vis-à-vis a generalization of a method indicating "family name" of compounds from which this specific compound is selected if the technical effect is different. In this context, the client is of the opinion that the effect of TGF- $\beta$ 1, TGF- $\beta$ 2 and TGF- $\beta$ 3 differs from a general description of the effect of the whole TGF- $\beta$  family. Therefore, it could be necessary to delimit the broad term TGF- $\beta$  to the specific members TGF- $\beta$ 1, TGF- $\beta$ 2 and TGF- $\beta$ 3 in claim 1.

6. Applicant requests reconsideration of the rejections under 35 USC 103. Referring to the combination of "Logan" and "Alexander", it seems to be possible to argue that it is not obvious to combine

"Logan" with "Alexander", since "Alexander" does not teach the treatment of cerebral neuronal diseases but teaches an agent effective for lysis of acute induced venous sinus thrombosis (cf. The abstract of "Alexander". Therefore, a person skilled in the art would not take "Alexander" for a combination with "Logan".

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

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Enclosure

MARKED-UP VERSION OF CLAIM AMENDMENTS

1. A method for [Use of a compound capable of substantially]  
inhibiting the biological activity of [TGF-] transforming growth  
factor  $\beta$  on predamaged neurons, [for the preparation of a  
medicament for treating cerebral disorders] said method comprising  
treating said predamaged neurons with a compound inhibiting the  
biological activity of TGF- $\beta$ .